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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/621,725	03/21/1996	PAUL V. LEHMANN	CASE-02138	1344

23535 7590 05/03/2004

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EXAMINER	
SCHWADRON, RONALD B	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/621,725	LEHMANN ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 25-45* is/are pending in the application.

4a) Of the above claim(s) *28-31,36-39 and 42-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,25-27,32-35,40,41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Applicant's election of the species IL-5 in the paper received 2/9/2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 28-31,36-39,42-45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the paper received 2/9/2004.

3. Claims 1,25-27,32-35,40,41 are under consideration.

4. References not considered on the IDS filed 10/20/2003 were not considered because a copy of the reference was not included or the citation was incomplete (Swierkosz et al., lacked year published) or the reference was incomplete (Male et al.).

5. The rejection of claim 1 and 25 under 35 U.S.C 102(e) as anticipated by Muir et al. for the reasons elaborated in the previous Office Action is withdrawn in view of the amended claims.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1,25-27,32-35,40,41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the method of claim 1, part b) or claim 25, part b) or claim 26, part b) that does not include the additional

limitation "under conditions such that said symptoms are reduced". Regarding applicants comments, support for said claim is not found in pages 16 or 17 of the specification. There is also no support in the specification as originally filed for the method of claim 1, part d) or claim 25 part d). Regarding applicants comments, said limitation is not disclosed in pages 16 or 17 of the specification. Said pages disclose an experiment wherein specific cytokine are measured in mice treated with MBP in IFA. This is not a disclosure of the method of claim 1, part d) or claim 25 part d). There is no support in the specification as originally filed for the scope of the claimed inventions (eg. the claimed invention constitute new matter).

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1,25,34,40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muir et al. (US Patent 5,891,435) in view of Falcone et al.

Muir et al. teach immunization of humans with MBP to prevent/ameliorate MS wherein the adjuvant IFA is used (see column 9, last paragraph, column 10, column 6, column 8, lines 8-12, and column 13, lines 13-15). Muir et al. teach immunization of humans with insulin to prevent/ameliorate diabetes (eg. a disease having autoimmune destruction of pancreatic islet cells) wherein the adjuvant IFA is used (see claims). Muir et al. teach that said treatment can be applied to patients suffering from autoimmune

disease (see column 6, lines 13-15). Patients suffering from autoimmune disease would already exhibit symptoms of autoimmune disease. Muir et al. do not teach the particular assay method recited in the claims. Falcone et al. teach that immunization of mice with "immunogenic proteins" in IFA is used to treat EAE and leads to the production of Th2, wherein the presence of Th2 is determined in an ELISPOT assay measuring IL-4 as an indication of Th2 (see abstract). Falcone et al. teach that IL-4 is measured in an immunoassay to detect the presence of Th2. Since immunization with "immunogenic protein" in IFA and immunization with MBP in IFA can be both use to treat MS/EAE, it would be reasonable to conclude that both treatments induce Th2. Furthermore, MBP is an immunogenic protein (eg. it induces an autoimmune response). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Falcone et al. teach that immunization of mice with immunogenic protein in IFA is used to treat EAE and leads to the production of Th2, wherein the presence of Th2 is determined in an ELISPOT assay measuring IL-4 as an indication of Th2 and Muir et al. teach immunization of humans with MBP to prevent/ameliorate MS wherein the adjuvant IFA is used. One of ordinary skill in the art would have been motivated to do the aforementioned because Falcone et al. teach that immunization of mice with immunogenic protein in IFA is used to treat EAE and leads to the production of Th2, wherein the presence of Th2 is determined in an ELISPOT assay measuring IL-4 as an indication of Th2 and similar procedures would have been used to detect Th2 in humans. The absence of Il-4 or low levels of IL-4 would indicate that the cells were Th1. The assay could have used T cells derived from any source in the animal (eg. primary cultures or cloned T cells, etc).

Regarding applicants comments, Falcone et al. teach that immunization of mice with immunogenic protein in IFA is used to treat EAE and leads to the production of Th2, wherein the presence of Th2 is determined in an ELISPOT assay measuring IL-4 as an indication of Th2 (see abstract). The EAE model is the same animal model as used by applicant in the specification. Regarding applicants comments, the Muir et al. patent is considered enabled in the absence of evidence establishing a prima facie case to the contrary. Applicant has not provided such evidence. The mere absence of a specific working example does not in itself establish that a reference is not enabled. Furthermore, Muir et al. teach immunization of humans with insulin to

prevent/ameliorate diabetes (eg. a disease having autoimmune destruction of pancreatic islet cells) wherein the adjuvant IFA is used (see claims, wherein the claims of an issued US Patent are considered enabled). Regarding applicants other comments about assay steps recited in the claims, Falcone et al. teach that immunization of mice with immunogenic protein in IFA is used to treat EAE and leads to the production of Th2, wherein the presence of Th2 is determined in an ELISPOT assay measuring IL-4 as an indication of Th2 (see abstract).

10. Claims 35,41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muir et al. (US Patent 5,891,435) in view of Falcone et al. as applied to claims 1,25,34,40 above, and further in view of Vieira et al. (US Patent 6,106,823).

The previous rejection renders obvious the claimed invention except for detection of IL-5 as the cytokine indicative of the presence of Th2. Vieira et al. teach that both IL-4 and IL-5 are secreted by Th2 (see column 9, third paragraph from bottom). Therefore, the detection of IL-5 could also be used to indicate the presence of Th2. Assays for detecting IL-5 were known in the art (see Vieira et al., Example 8). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection renders obvious the claimed invention except for detection of IL-5 as the cytokine indicative of the presence of Th2 whilst Vieira et al. teach that both IL-4 and IL-5 are secreted by Th2 and therefore the detection of IL-5 could also be used to indicate the presence of Th2.

11. Claims 26,32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muir et al. (US Patent 5,891,435) in view of Falcone et al. as applied to claims 1,25,34,40 above, and further in view of Goodwin et al. (US Patent 5,569,585), Oprandy (US Patent 5,200,312).

The cited rejection renders obvious the claimed invention except for use of the particular assay method recited in the claims using a hydrophobic membrane. Falcone et al. teach that immunization of mice with immunogenic protein in IFA is used to treat EAE and leads to the production of Th2, wherein the presence of Th2 is determined in an ELISPOT assay measuring IL-4 as an indication of Th2 (see abstract). ELISA assays for T cell cytokines are known in the art including "sandwich" type assays that use a

capture antibody and a labeled probe antibody (see Goodwin et al., column 10, and Oprandy, see abstract). Oprandy teaches the use of antibody coated PVDF membranes (eg. a hydrophobic membrane) in immunoassays (see column 3 and Example 1). Oprandy teaches that the use of antibody coated PVDF membranes in immunoassays results in improved sensitivity (see column 3, first paragraph). Falcone et al. teach that IL-4 is measured in an immunoassay to detect the presence of Th2. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Falcone et al. teach that immunization of mice with immunogenic protein in IFA is used to treat EAE and leads to the production of Th2, wherein the presence of Th2 is determined in an ELISPOT assay measuring IL-4 as an indication of Th2, Muir et al. teach immunization of humans with MBP to prevent/ameliorate MS wherein the adjuvant IFA is used, ELISA assays for T cell cytokines were known in the art and Oprandy teaches that the use of antibody coated PVDF membranes in immunoassays results in improved sensitivity. One of ordinary skill in the art would have been motivated to do the aforementioned because Falcone et al. teach that immunization of mice with immunogenic protein in IFA is used to treat EAE and leads to the production of Th2, wherein the presence of Th2 is determined in an ELISPOT assay measuring IL-4 as an indication of Th2 and similar procedures would have been used to detect Th2 in humans . One of ordinary skill in the art would have been also been motivated to do the aforementioned because Oprandy teaches that the use of antibody coated PVDF membranes in immunoassays results in improved sensitivity.

12. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Muir et al. (US Patent 5,891,435) in view of Falcone et al. and Goodwin et al. (US Patent 5,569,585) and Oprandy (US Patent 5,200,312) as applied to claims 1,25,26,32,34,40 above, and further in view of Vieira et al. (US Patent 6,106,823).

The previous rejection renders obvious the claimed invention except for detection of IL-5 as the cytokine indicative of the presence of Th2. Vieira et al. teach that both IL-4 and IL-5 are secreted by Th2 (see column 9, third paragraph from bottom). Therefore, the detection of IL-5 could also be used to indicate the presence of Th2. Assays for detecting IL-5 were known in the art (see Vieira et al., Example 8). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made

]to have created the claimed invention because the previous rejection renders obvious the claimed invention except for detection of IL-5 as the cytokine indicative of the presence of Th2 whilst Vieira et al. teach that both IL-4 and IL-5 are secreted by Th2 and therefore the detection of IL-5 could also be used to indicate the presence of Th2.

13. Claims 26,33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muir et al. (US Patent 5,891,435) in view of Falcone et al. as applied to claims 1,25,34,40 above, and further in view of Goodwin et al. (US Patent 5,569,585), Thorpe et al. (US Patent 5,855,866) and Anderson et al. (US Patent 4,747,919).

The cited rejection renders obvious the claimed invention except for use of the particular assay method recited in the claims using an enclosed bottom hydrophobic membrane. ELISA assays for T cell cytokines are known in the art including "sandwich" type assays that use a capture antibody and a labeled probe antibody (see Goodwin et al., column 10)). Thorpe et al. teaches the use of antibody coated PVC solid bottom microtiter plates in ELISA assays for detecting cytokines (see column 13, second paragraph, column 24, first complete paragraph and column 42, penultimate paragraph, wherein there is no filtration step in the disclosed assay). Conventional microtiter plates can have a flat bottom (for example see Goodwin et al., column 19, last paragraph). PVC is a hydrophobic material (see Anderson et al., column 4, second complete paragraph). The PVC microtiter plate comprises a "hydrophobic membrane" (eg. the plate is made of PVC). Thorpe et al. teach that said plate can be used in an ELISA to measure the cytokines recited detected by the anticytokine antibodies recited in claim 4 (see column 13, second paragraph). Falcone et al. teach that IL-4 is measured in an immunoassay to detect the presence of Th2. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection renders obvious the claimed invention except for use of the particular assay method recited in the claims using an enclosed bottom hydrophobic membrane, whilst ELISA assays for T cell cytokines were known in the art and Thorpe et al. teaches that the use of antibody coated hydrophobic PVC microtiter plates. One of ordinary skill in the art would have been motivated to do the aforementioned because Falcone et al. teach that immunization of mice with

immunogenic protein in IFA is used to treat EAE and leads to the production of Th2, wherein the presence of Th2 is determined in an ELISPOT assay measuring IL-4 as an indication of Th2 and similar procedures would have been used to detect Th2 in humans . One of ordinary skill in the art would have also been motivated to do the aforementioned because Thorpe et al. disclose the use of an ELISA to measure the cytokines recited detected by the anticytokine antibodies recited in claim 4 (see column 13, second paragraph). As per above, the use of hydrophobic (eg. PVC) solid bottom microtiter plates was common in the art at the time the invention was made.

14. Claims 1,25,34,35,40,41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Forsthuber et al. in view of Muir et al. (US Patent 5,891,435) .

Forsthuber et al. disclose that injection of MBP in IFA induces a vigorous Th2 response and can be used to treat to treat EAE(see abstract). The Forsthuber et al. reference refers to treatment of EAE in mice (see penultimate sentence). Forsthuber et al. teach that primary cell cultures of treated mouse cells are assayed for the secretion of IL-5 (Th2 cytokine) or IFNgamma (Th1) wherein the presence of the IL-5 indicated Th2 and the presence of IFNgamma indicated Th1. Forsthuber et al. do not specifically teach that humans were immunized with MBP and assayed for the presence of Th2. EAE is an art known model for MS in humans. Muir et al. teach immunization of humans with MBP to prevent/ameliorate MS wherein the adjuvant IFA is used (see column 9, last paragraph, column 10, column 6, column 8, lines 8-12, and column 13, lines 13-15). Muir et al. teach immunization of humans with insulin to prevent/ameliorate diabetes (eg. a disease having autoimmune destruction of pancreatic islet cells) wherein the adjuvant IFA is used (see claims). Muir et al. teach that said treatment can be applied to patients suffering from autoimmune disease (see column 6, lines 13-15). Patients suffering from autoimmune disease would already exhibit symptoms of autoimmune disease. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Forsthuber et al. teach the claimed invention except for applying it to humans whilst Muir et al. teach immunization of humans with MBP to prevent/ameliorate MS wherein the adjuvant IFA is used. One of ordinary skill in the art would have been motivated to do the aforementioned to monitor for the presence of Th2 in humans to determine the efficacy of the particular immunization protocol used.

15. Claims 26,32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Forsthuber et al. in view of Muir et al. (US Patent 5,891,435) as applied to claims 1,25,34,35,40,41 and further in view of Goodwin et al. (US Patent 5,569,585), Oprandy (US Patent 5,200,312).

The previous rejection renders obvious the claimed invention except for use of the particular assay method recited in the claims using a hydrophobic membrane. ELISA assays for T cell cytokines are known in the art including "sandwich" type assays that use a capture antibody and a labeled probe antibody (see Goodwin et al., column 10, and Oprandy, see abstract). Oprandy teaches the use of antibody coated PVDF membranes (eg. a hydrophobic membrane) in immunoassays (see column 3 and Example 1). Oprandy teaches that the use of antibody coated PVDF membranes in immunoassays results in improved sensitivity (see column 3, first paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Forsthuber et al. teach that immunization of mice with MBP in IFA is used to treat EAE and leads to the production of Th2, Muir et al. teach immunization of humans with MBP to prevent/ameliorate MS wherein the adjuvant IFA is used, ELISA assays for T cell cytokines were known in the art and Oprandy teaches that the use of antibody coated PVDF membranes in immunoassays results in improved sensitivity. One of ordinary skill in the art would have been motivated to do the aforementioned because Forsthuber et al. teach that immunization of mice with MBP in IFA is used to treat EAE and leads to the production of Th2, wherein the presence of Th2 is determined in an assay measuring IL-5 as an indication of Th2 and similar procedures would have been used to detect Th2 in human. One of ordinary skill in the art would have been also been motivated to do the aforementioned because Oprandy teaches that the use of antibody coated PVDF membranes in immunoassays results in improved sensitivity.

16. Claims 26,33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Forsthuber et al. in view of Muir et al. (US Patent 5,891,435) as applied to claims 1,25,34,35,40,41 and further in view of Goodwin et al. (US Patent 5,569,585), Thorpe et al. (US Patent 5,855,866) and Anderson et al. (US Patent 4,747,919).

The cited rejection renders obvious the claimed invention except for use of the particular assay method recited in the claims using an enclosed bottom hydrophobic membrane. ELISA assays for T cell cytokines are known in the art including "sandwich" type assays that use a capture antibody and a labeled probe antibody (see Goodwin et al., column 10)). Thorpe et al. teaches the use of antibody coated PVC solid bottom microtiter plates in ELISA assays for detecting cytokines (see column 13, second paragraph, column 24, first complete paragraph and column 42, penultimate paragraph, wherein there is no filtration step in the disclosed assay). Conventional microtiter plates can have a flat bottom (for example see Goodwin et al., column 19, last paragraph). PVC is a hydrophobic material (see Anderson et al., column 4, second complete paragraph). The PVC microtiter plate comprises a "hydrophobic membrane" (eg. the plate is made of PVC). Thorpe et al. teach that said plate can be used in an ELISA to measure the cytokines recited detected by the anticytokine antibodies recited in claim 4 (see column 13, second paragraph). Forsthuber et al. teach that IL-5 is measured in an immunoassay to detect the presence of Th2. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection renders obvious the claimed invention except for use of the particular assay method recited in the claims using an enclosed bottom hydrophobic membrane, whilst ELISA assays for T cell cytokines were known in the art and Thorpe et al. teaches that the use of antibody coated hydrophobic PVC microtiter plates. One of ordinary skill in the art would have been motivated to do the aforementioned because Forsthuber et al. teach that immunization of mice with MBP in IFA is used to treat EAE and leads to the production of Th2, wherein the presence of Th2 is determined in an ELISPOT assay measuring IL-4 as an indication of Th2 and similar procedures would have been used to detect Th2 in humans . One of ordinary skill in the art would have also been motivated to do the aforementioned because Thorpe et al. disclose the use of an ELISA to measure the cytokines recited detected by the anticytokine antibodies recited in claim 4 (see column 13, second paragraph). As per above, the use of hydrophobic (eg. PVC) solid bottom microtiter plates was common in the art at the time the invention was made.

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached Monday to Thursday, 7:30am to 6:00pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at 571 272 0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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